General

Guideline Title

Congress of Neurological Surgeons systematic review and evidence-based guideline on pretreatment ophthalmology evaluation in patients with suspected nonfunctioning pituitary adenomas.

Bibliographic Source(s)

Newman SA, Turbin RE, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on pretreatment ophthalmology evaluation in patients with suspected nonfunctioning pituitary adenomas. Neurosurgery. 2016 Oct;79(4):E530-2. [20 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The rating schemes used for the strength of the evidence (Class I-III) and the levels of recommendation (Level I-III) are defined at the end of the "Major Recommendations" field.

Question

What is the role of ophthalmologic evaluation in pretreatment assessment of nonfunctioning adenoma patients?

Level III Recommendation

Pretreatment evaluation of nonfunctioning pituitary adenoma (NFPA) patients by an ophthalmologist is recommended. Ophthalmologic evaluation identifies patients with asymptomatic visual deficits due to the ophthalmologist's ability to quantitate psychophysical (acuity and visual fields), functional (quantitation of afferent pupillary defect and visual evoked potentials [VEP]), and anatomical (disc appearance and ocular coherence tomography [OCT]) assessment. Ophthalmologic evaluation may also provide prognostic factors for recovery and, when paired with postoperative evaluation, documents postoperative change.

Question

Are there ophthalmologic tests of particular value in the pretreatment assessment of nonfunctioning adenoma patients?

Level III Recommendations

- Automated static perimetry is recommended for early detection of visual field deficits, many of which the patient will be unaware of, in patients with nonfunctioning pituitary adenomas. Automated static perimetry, even with a standard III size test object, will often pick up subtle bitemporal visual field defects, less commonly homonymous defects, and, infrequently, arcuate defects characteristic of optic nerve pathology.
- Visual evoked potentials may be used to assess the optic nerves in nonfunctioning pituitary adenoma patients in a manner that may correlate with visual field deficits, but false positives and negatives may limit this testing to cases in which psychophysical areas, such as acuity and visual fields, cannot be assessed.

Question

Are there preoperative prognostic factors associated with the chances of postoperative vision improvement after nonfunctioning adenoma resection that can inform patients and their providers?

Level III Recommendations

- It is recommended that older patients and patients with longer duration (>4 months) of vision loss be counseled regarding the reduced chance of postoperative vision improvement.
- Formal ophthalmologic examination, looking for optic nerve atrophy or OCT to measure both retinal nerve fiber layer (RNFL) thickness and the presence of damage to the ganglion cell layer on algorithms that segment the macular cube, is recommended to assess a patient's chances of postoperative vision improvement.
- Although not yet standard of practice, anatomic assessment of the anterior visual pathways provided with the use of optical coherence tomography documents previous damage, showing evidence of nerve fiber bundle thinning and evidence of ganglion cell dropout with segmentation analysis.

Definitions

Evidence Classification for Clinical Assessment Studies

Class I	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.60. The Kappa statistic is defined as (po-pe)/(1-pe) where po is the relative observed agreement and pe is the hypothetical probability of chance agreement.
Class II	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.40
Class III	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic <0.40

Evidence Classification for Prognostic Studies

In order to evaluate papers addressing prognosis, five technical criteria are applied:

- Was a well-defined representative sample of patients assembled at a common (usually early) point in the course of their disease?
- Was patient follow-up sufficiently long and complete?
- Were objective outcome criteria applied in a "blinded" fashion?
- If subgroups with different prognoses were identified, was there adjustment for important prognostic factors?
- If specific prognostic factors were identified, was there validation in an independent "test set" group of patients?

Class I - All 5 technical criteria above are satisfied

Class II - Four of five technical criteria are satisfied

Class III - Everything else

Evidence Classification for Therapeutic Studies

Class I	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II	Evidence provided by well-designed observational studies with concurrent controls (e.g. case control and cohort studies)

Class III	Evidence provided by expert opinion, case series, case reports and studies with historical controls

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nonfunctioning pituitary adenoma (NFPA) with visual disturbances, including visual field defects, loss of central vision, and motility problems

Guideline Category

Counseling

Evaluation

Clinical Specialty

Endocrinology

Neurological Surgery

Neurology

Oncology

Ophthalmology

Intended Users

Physicians

Guideline Objective(s)

To establish recommendations related to preoperative assessment of vision in nonfunctioning adenoma patients

Target Population

Adult patients with nonfunctioning pituitary adenomas (NFPA)

Interventions and Practices Considered

1. Pretreatment evaluation of nonfunctioning pituitary adenoma (NFPA) patients by an ophthalmologist
2. Automated static perimetry
3. Visual evoked potentials
4. Counseling patients on the reduced chance of postoperative vision improvement
5. Formal ophthalmologic examination looking for optic nerve atrophy or optical coherence tomography (OCT) changes
6. Anatomic assessment of the anterior visual pathways

Major Outcomes Considered

- Sensitivity and specificity of tests
- Presence of visual symptoms/defects

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Search Strategy

Literature Search

The guideline task force collaborated with a medical librarian to search for articles published from January 1, 1966, to October 1, 2014. Searches were conducted in two electronic databases, PubMed and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by the guideline task force members and medical/research librarians using previously published search strategies to identify relevant studies. The root search strategies are provided in Appendix A of the introduction and methodology companion and the chapter-specific search strategies are provided in the appendix of the full version of the guideline (see the "Availability of Companion Documents" field).

The searches of electronic databases were supplemented with manual screening of the bibliographies of all retrieved publications. The bibliographies of recent systematic reviews and other review articles for potentially relevant citations were also screened. All articles identified were subject to the study selection criteria listed below. The guideline task force also examines lists of included and excluded studies for errors and omissions.

Article Inclusion Criteria

Articles were retrieved and included only if they met specific inclusion criteria. These criteria were also applied to articles provided by the evidence-based clinical practice guideline task force members who supplemented the electronic database searches with manual searches of the bibliographies. To reduce bias, these criteria were specified *a priori* before conducting the literature searches. For the purposes of this guideline, articles had to meet the following criteria to be included as evidence to support the recommendations presented in this guideline:

- Investigated patients suspected of having a pituitary mass
- Enrolled patients ≥18 years of age
- Either enrolled exclusively nonfunctioning pituitary adenoma (NFPA) patients OR combined the results of patients with NFPAs and functioning pituitary adenomas and/or other pituitary masses with ≥90% of the patients having NFPAs
- Was a full article report of a clinical study
- If a prospective case series, reported baseline values

- Appeared in a peer-reviewed publication
- Enrolled ≥10 NFPA patients per arm per intervention (20 total) for each outcome
- Was of humans
- Was published in or after 1966
- Quantitatively presented results

Article Exclusion Criteria

Articles of the following types were excluded as evidence to support the recommendations presented in this guideline:

- In vitro studies
- Studies performed on cadavers
- Studies not published in English
- Medical records reviews, meeting abstracts, historical articles, editorial, letters, or commentaries
- Systematic reviews, meta-analyses, or guidelines developed by others

Specific Methods for This Guideline

Literature Search

The task force collaborated with a medical librarian to search for articles published from January 1, 1966, to October 1, 2014. Two electronic databases were searched, PubMed and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by the evidence-based clinical practice guideline taskforce members and the medical librarian using previously published search strategies to identify relevant studies (see Appendix A in the full guideline).

Study Selection

The searches resulted in 447 articles, of which a total of 96 were recalled for full-text review. Ninety studies were excluded following full-text review.

Number of Source Documents

Six studies met the inclusion criteria and are included as evidence to support the guideline.

See Figure 1 in the full version of the guideline for the flowchart summarizing study selection (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

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Class I	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic ≥0.60. The Kappa statistic is defined as (po-pe)/(1-pe) where po is the relative observed agreement and pe is the hypothetical probability of chance agreement.
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Class III	Evidence provided by expert opinion, case series, case reports and studies with historical controls

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Rating the Quality of the Evidence and Levels of Recommendations

The quality and classification of evidence (see the "Rating Scheme for the Strength of the Evidence" field) was rated using an evidence hierarchy developed by the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Guidelines Committee for each of four different study types: therapeutic, prognostic, diagnostic, and economic or decision modeling. The methodology used to conduct quality evaluations of the evidence can be located on the CNS Web site (see also the "Availability of Companion Documents" field). The level/strength of recommendation (i.e., Level I, II, or III) was linked to the quality of the overall body of evidence included in the chapter and in support of a given recommendation.

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

Process Overview

A multidisciplinary task force comprised of physician volunteers and evidence-based medicine trained methodologists conducted a systematic review of the literature relevant to the management of non-functioning pituitary adenomas (NFPAs). The physician volunteers represented neurosurgeons, neuro-ophthalmologists, neuroradiologists, and endocrinologists with expertise in pituitary adenomas. The evidence-based medicine trained methodologists had previous experience in guidelines production for the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). During the development process, the task force participated in a series of conference calls and meetings. Multiple iterations of written review were conducted by the individuals of the panel and various CNS/AANS Committees prior to approval.

Guideline Task Force Panel Consensus

The guideline task force panel included context experts from multiple disciplines and various areas of therapy to address the topics addressed in

this guideline. Sub-task force members were assigned to a specific chapter and were involved in the literature review, the creation and editing of the evidence tables, reviewing and voting of the final recommendations.

Voting on the Recommendations

The task force used a structured voting technique to finalize and approve the final recommendations, language, and strength of recommendations, presented in this review. The voting technique is referred to as the nominal group technique. This technique includes up to three rounds of voting, using secret ballots to ensure task force members are blinded to the responses of other task force members. All the recommendations in this review were approved following the first round of voting and no further discussion was needed to finalize the recommendations. During the course of editing and finalization of the document, changes were made to allow recommendations to conform to the rules of evidence and language as described above. When this occurred, the changes were reviewed and approved by the group.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations Rating Scheme

Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)

Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)

Level III: Clinical uncertainty (inconclusive or conflicting evidence or opinion)

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Guideline Approval Process

The guideline draft was circulated to the entire task force for final review and approval prior to submission for peer review by the Joint Guidelines Committee (JGC) of the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS). Due to the reviewers' knowledge of evidence-based medicine and clinical practice guidelines methodology training, the JGC peer reviewers served as the journal's editorial reviewers. As a part of the JGC review process, the reviewers provided input on the content of the guideline and suggested revisions prior to approval and endorsement of the draft guideline by the CNS and AANS prior to publication. The development of this guideline was editorially independent from the funding agencies (CNS Executive Committee, and AANS/CNS Joint Tumor Section Executive Committee), the CNS and Joint Tumor Section.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field). All of the evidence was Class III.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Maintenance of visual function remains critical to a patient's health and well-being. As nonfunctioning pituitary adenomas frequently present with visual symptoms, it is imperative that neurosurgeons be aware of the symptoms and how they can be best quantitated and followed. The advent of more quantitative assessment, both of psychophysics and of anatomy, will likely influence thinking about these tumors in the future.
- Preoperative assessment of a nonfunctioning adenoma patient by a neuro-ophthalmologist provides important insight into patients previously felt to be asymptomatic and, when performed without delaying surgery, offers valuable objective insight into the exact nature of a patient's visual deficit and prognostic insight into the chances of postoperative visual improvement.
- Models at some institutions recognize the importance of multidisciplinary assessment including ophthalmologic, endocrine, and radiographic studies to optimize care for all pituitary patients.

Potential Harms

Visual evoked potentials may render false-positive and false-negative results, which limits this testing to cases in which psychophysical areas, such as acuity and visual fields, cannot be assessed.

Qualifying Statements

Qualifying Statements

Qualifying Statements

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. The presentations are designed to provide an accurate review of the subject matter covered. This guideline is disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in its development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a physician should be sought. The recommendations contained in this guideline may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in this guideline must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Limitations

This review of the literature revealed no Class I data concerning nonfunctioning pituitary adenomas and visual findings, although conducting a double blinded randomized control trial would be very difficult to undertake due to the strict criteria surrounding such a trial and the nature of the disease and variations in the time at which patients are diagnosed. The non-comparative case series that were identified also lacked sufficient duration of follow-up or sufficient rigorous quantitative assessment to be considered Class II evidence based on the definitions utilized. For example, many studies failed to report their method of assessing visual acuity, and even fewer emphasized the importance of best corrected acuity to avoid contamination with other visual reasons for decreased acuity. Often, visual function is said to return to "normal" without criteria. Very few papers had all patients seen by an ophthalmologist, although this is likely a reflection of the challenges involved in making such arrangements. Many studies present cursory visual information while focusing on the safety of the reported treatment technique. When mentioned, acuity improvement has been stated as "significant" with a one-line improvement in function. Authors suggest the use of uncorrected visual acuity.

Another challenge is finding a quantitative means of assessing extrafoveal (visual field) visual function. There is often no data on distinguishing homonymous from "quadrantic" defects. Some studies have reported visual fields based initially on confrontation with quantitative data only on follow-up Other retrospective studies include patients with only confrontation or near vision data. While most recent studies now utilize automated static perimetry, some still report Goldmann perimetry, and even when using automated fields there is no universal agreement on the platform used and even less agreement on comparing visual fields. Some authors have come up with their own scoring system for perimetry. Several studies report "normalization" or "complete resolution" of visual fields without defining criteria. Some studies have suggested minimal changes in grey scale of automated perimetry to be significant.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Newman SA, Turbin RE, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on pretreatment ophthalmology evaluation in patients with suspected nonfunctioning pituitary adenomas. Neurosurgery. 2016 Oct;79(4):E530-2. [20 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Oct

Guideline Developer(s)

Congress of Neurological Surgeons - Professional Association

Source(s) of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Tumor Section of the Congress of Neurological Surgeons and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Guideline Committee

Nonfunctioning Pituitary Adenoma Guideline Task Force

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Potential Conflicts of Interest

All Nonfunctioning Pituitary Adenoma (NFPA) Guideline Task Force members were required to disclose all potential conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guidelines Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of Task Force Members with possible conflicts and restrict the writing, reviewing and/or voting privileges of that person to topics that are unrelated to the possible COIs.

Disclosures

Roger E.Turbin, MD, owns stock in Titan Medical, Inc., Ocata Therapeutics, Inc., and Biogen, Inc.

The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Guideline Endorser(s)

American Association of Neurological Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Neurosurgery Web site . Also available in ePub format from the Neurosurgery Web site .

Availability of Companion Documents

The following are available:

- Newman SA, Turbin RE, Bodach ME, Tumialan LM, Oyesiku NM, Litvack Z, Zada G, Patil CG, Aghi MK. Congress of Neurological Surgeons systematic review and evidence-based guideline on pretreatment ophthalmology evaluation in patients with suspected nonfunctioning pituitary adenomas. Full guideline. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 21 p. Available from the Congress of Neurological Surgeons (CNS) Web site .
- Aghi MK, Chen CC, Fleseriu M, Newman SA, Lucas JW, Kuo JS, Barkhoudarian G, Farrell CJ, Sheehan J, Ziu M, Dunn IF. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: executive summary. Neurosurgery. 2016 Oct;79(4):521-3. Available from the Neurosurgery Web site .
- Aghi MK, Bodach ME, Tumialan LM, Oyesiku NM, Patil CG, Litvack Z, Zada G. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of patients with nonfunctioning pituitary adenomas: introduction and methodology. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2016 Oct. 12 p. Available from the CNS Web site .
- Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. Available from the CNS Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 10, 2017. The information was verified by the guideline developer on February 22, 2017.

Copyright Statement

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